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Dichlorvos-induced hepatotoxicity in rats and the protective effects of vitamins C and E

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ABSTRACT

Dichlorvos is an organophosphate insecticide that is widely used in pest control. Vitamin C (200 mg/kg) + vitamin E (200 mg/kg), dichlorvos (1.6 mg/kg), or a combination of vitamin C (200 mg/kg) + vitamin E (200 mg/kg) + dichlorvos (1.6 mg/kg) was given to rats via oral gavage for 7 weeks. When rats of the dichlorvos-treated group and the vitamins + dichlorvos-treated group were compared with the control group, body weights were decreased and liver weights were increased significantly at the end of the 4th and 7th week. Serum total protein, albumin, triglyceride, low density lipoprotein-cholesterol (VLDL-cholesterol) levels were decreased, and serum alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyl-transferase (GGT), lactate dehydrogenase (LDH), and total cholesterol levels were increased significantly at the end of the 4th and 7th week in the dichlorvos- and vitamins + dichlorvos-treated rats. There was a statistically significant difference for all biochemical parameters when the vitamins + dichlorvos-treated group was compared with the dichlorvos-treated group at the end of the 4th and 7th week. In an electron microscopic investigation, swelling of mitochondria and dilatation of endoplasmic reticulum were observed in liver cells of the dichlorvos- and vitamins + dichlorvos-treated rats at the end of the 4th and 7th week. As a result, vitamins C and E reduced dichlorvos hepatotoxicity, but vitamins C and E did not confer complete protection.

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1. Introduction

For centuries, pesticides have been used in agriculture to enhance food production by eradicating unwanted insects and controlling disease vectors (Prakasam et al., 2001). Among common pesticides, organophosphorus (OP) compounds are widely used in agriculture, medicine, and industry (Storm et al., 2000). The primary site of action of organophosphate pesticides is the central and peripheral nervous systems because they inhibit acetylcholinesterase (AChE), the enzyme that hydrolyses the neurotransmitter acetylcholine (ACh). In the presence of an inhibitor of AChE, synaptic ACh may increase to abnormally high concentrations, which is postulated to precipitate a “cholinergic crisis” that can be debilitating and possibly fatal (Sarkar et al., 2000). Furthermore, OP pesticides are known to cause inhibition of pseudocholinesterase activity (Kalender et al., 2006). Other systems that could be affected by OP intoxicants are pancreas (Yürümez et al., 2007), liver (S. Kalender et al., 2005), heart (Ogutcu et al., 2006), kidney (Kalender et al., 2007), and reproductive system (Uzunhisarcikli et al., 2007).

Dichlorvos (2,2-dichlorovinyl dimethyl phosphate; DDVP) is an organophosphate compound and is one of the most widely used pesticides for the control of household pests, public health pests, and stored product insect infestations (Celik et al., 2008). Dichlorvos is a direct-acting inhibitor of AChE (WHO, 1989), the enzyme that degrades the neurotransmitter ACh in cholinergic synapses, and disrupts nerve function that can end in the death of the organism (Varo et al., 2003). Dichlorvos is effective against mushroom flies, aphids, spider mites, caterpillars, thrips, and white flies in greenhouses, outdoor fruit, and vegetable crops (Yarsan and Cakir, 2006; Celik et al., 2008). Exposure of the general public to dichlorvos may occur via air, water, or food because it is readily absorbed through all routes of exposure (Raheja and Gill, 2002). Dichlorvos exposure has been linked to substantial adverse health effects on several organ systems, including the respiratory system (Atiş et al., 2002) and reproductive system (Okamura et al., 2005; Oral et al., 2006).

Both vitamins C and E have been used in pesticide toxicity studies (Kalender et al., 2007; Uzunhisarcikli et al., 2007). Many insecticides are hydrophobic molecules which bind extensively to biological membranes, especially to phospholipid bilayers (Lee et al., 1991). Vitamin E is the major lipid-soluble antioxidant and protects cellular membranes and lipoproteins against peroxidation (Yavuz et al., 2004). Studies carried out with antioxidants

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such as α-tocopherol have shown inhibition of free radical formation (Kalender et al., 2004; Y. Kalender et al., 2005), which may effectively minimize lipid peroxidation in biological systems (Kalender et al., 2002). The reaction of α-tocopherol with free radicals generates tocopherol radicals. Vitamin C (ascorbic acid) is a low molecular weight antioxidant that defends the cellular compartment against water-soluble oxygen nitrogen radicals. It is an effective antioxidant of the hydrophilic phase (Jurczuk et al., 2007). Furthermore, vitamin C can restore the antioxidant abilities of vitamin E, suggesting that a major function of ascorbic acid is to recycle the tocopheroxyl radical (Serbecic and Beutelspacher, 2005).

The aim of this study was to investigate for pathological changes of the liver of rats after a 4-week (subacute exposure) and a 7-week (subchronic exposure) exposure to dichlorvos and to assess the protective potential of vitamins C and E.

2. Materials and methods

2.1. Animals

Forty-eight adult male Wistar rats weighing between 310 and 340 g were obtained from the Refik Saydam Central Hygiene Institute, Ankara, Turkey. The animals were housed in plastic cages and fed a standard laboratory diet and water *ad libitum*. Rats were exposed to a 12 h light/dark cycle at a room temperature of 18–22 °C. Animals were quarantined for 10 days before beginning the experiments. All rats were handled in accordance with the standard guide for the care and use of laboratory animals.

2.2. Chemicals

Dichlorvos (purity 98%) was obtained from the Agricultural Struggle Center, Ankara, Turkey. Vitamin E (DL-α-tocopherol acetate) was supplied by Merck (Germany) and vitamin C (L-ascorbic acid) was supplied by Carlo Erba (Milano, Italy).

2.3. Animal treatment schedule

Rats were randomly divided into two groups: a control group ($n = 12$) and an experimental group ($n = 36$). Rats in the experimental group were then divided into three subgroups: vitamin C + vitamin E-treated group (vitamins-treated group, $n = 12$), dichlorvos-treated group ($n = 12$), and vitamins + dichlorvos-treated group ($n = 12$). At the end of the 4th and 7th week, six rats were anesthetized by inhalation of diethyl ether and then euthanized. Blood and tissue samples were taken for the biochemical and electron microscope investigations.

The treatments were administered in the morning (between 09:00 and 10:00 h) to non-fasted rats. The day of the first exposure to dichlorvos was delineated as experimental day 0.

2.3.1. Control group

Corn oil at a dose of 1 ml/kg body weight (bw) per day was given via oral gavage to rats once a day.

2.3.2. Vitamin C + vitamin E-treated group (vitamins-treated group)

Vitamin C (200 mg/kg bw per day) was administered via oral gavage to rats once a day. After vitamin C administration, vitamin E (200 mg/kg bw per day) was administered via oral gavage to rats once a day. Vitamins C and E were dissolved in water (1 ml/kg bw) and corn oil (1 ml/kg bw), respectively.

2.3.3. Dichlorvos-treated group

Dichlorvos was prepared at a dose of 1.6 mg/kg bw (1/50 LD_{50} oral dose) per day in corn oil and given via oral gavage to rats once a day.

2.3.4. Vitamins + dichlorvos-treated group

Vitamin C (200 mg/kg bw per day, once a day in water) and vitamin E (200 mg/kg bw per day, once a day in corn oil) were administered through oral gavage 30 min before the administration of dichlorvos (1.6 mg/kg bw per day, once a day in corn oil) via oral gavage.

2.4. Measurement of body and organ weights

Body and liver weights of the control and treated rats were measured at the end of the 4th and 7th week by employing an automatic balance (AND GX-600, Japan). Livers were removed from the adipose tissue before weighing. Rats were anesthetized with diethyl ether after measurement of body weights, and livers were removed and their weights were measured.

2.5. Biochemical evaluation

At the end of the 4th and 7th week, blood samples of the rats were taken from the heart and collected into sterile tubes. Blood samples were centrifugated at 3500 rpm for 20 min, and serum was separated. Livers were removed immediately and washed with sodium phosphate buffer (pH 7.2).

Total protein, albumin, total cholesterol, triglyceride, and VLDL-cholesterol (very low density lipoprotein-cholesterol) were assessed in serum using a commercially available spectrophotometric-enzymatic kit (Thermo Trace-BECGMAN, Germany) and analyzed by an autoanalyzer (Bayer ope-RA). ALP (alkaline phosphatase), ALT (alanine aminotransferase), AST (aspartate aminotransferase), GGT (γ-glutamyl-transferase), and LDH (lactate dehydrogenase) were assessed in serum with a commercially available enzymatic-kinetic kit (SpinReact-BECGMAN, Germany) and analyzed by autoanalyzer (Bayer ope-RA).

2.6. Transmission electron microscopy studies

For electron microscopic examinations of liver tissues, primary fixation was done in 3% glutaraldehyde in sodium phosphate buffer (200 mM, pH 7.2) for 3 h at 4 °C. Liver tissues were washed with the same buffer and postfixed in 1% osmium tetroxide (Agar Sci. Ltd.) in sodium phosphate buffer, pH 7.2, for 1 h at 4 °C. Tissue samples were washed with the same buffer for 3 h at 4 °C and then embedded in Araldite (Agar Sci. Ltd.). Thin sections were cut with a Leica EM UC6 (Leica Co., Austria) ultramicrotome. Samples were stained with 2% uranyl acetate and lead citrate. The sections were viewed and photographed on a Jeol 100CXII transmission electron microscope (Jeol Ltd., Japan) at 80 kV.

2.7. Statistical analyses

Data were analyzed using SPSS 11.0 for windows. Significance was calculated using one-way analyses of variance (ANOVA) followed by Tukeys procedure for multiple comparisons. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Evaluation of body and organ weights

Death was not observed in any of the experimental groups during the experimental period. However, food intake of the dichlorvos- and vitamins + dichlorvos-treated rats was reduced. Body weight, absolute liver weight, and relative liver weight did not significantly differ during the experimental between the vitamins-treated group and the control group.

At the end of the 4th and 7th week, there was a statistically significant decrease in body weight and an increase in the absolute and relative liver weights when the dichlorvos- and vitamins + dichlorvos-treated rats were compared to the control group ($P < 0.05$). When the vitamins + dichlorvos-treated group was compared to the dichlorvos-treated group, no statistically significant differences were observed for body weight or the absolute and relative liver weights at the end of the 4th and 7th week (Table 1).

3.2. Evaluation of biochemical results

The control group was compared with all other groups at the end of the 4th and 7th week. In addition to this, the dichlorvos-treated group was compared to the vitamins + dichlorvos-treated group. Biochemical changes are shown in Figs. 1–10. No statistically significant differences were observed when the vitamins-treated group was compared with the control group at the end of 4th and 7th week. The biochemical parameters were investigated in order to assess changes in hepatic function and changes in the lipid profile.

3.2.1. Changes in hepatic function

Total protein, albumin, ALP, ALT, AST, GGT, and LDH are indicators of hepatic function. There were statistically significant increases in ALP, ALT, AST, GGT, and LDH activities but statistically significant reductions in total protein and albumin levels in the dichlorvos- and vitamins + dichlorvos-treated groups compared to the control group at the end of the 4th and 7th week ($P < 0.05$) (Figs. 1–7).

Table 1
Body weight, liver weight, and relative liver weight of control and experimental rats

Groups	Body weight			Absolute liver weight (g)	Relative liver weight (g/100 g body weight)
	Initial (g)	Final (g)	%Change		
4th week					
Control	326.78 ± 1.72	347.57 ± 4.59	6.36 ± 0.85	12.71 ± 0.30	3.65 ± 0.04
Vitamins C and E	328.18 ± 2.17	352.82 ± 5.00	7.50 ± 0.86	13.09 ± 0.19	3.71 ± 0.01
Dichlorvos	326.95 ± 7.01	303.18 ± 4.74	−7.28 ± 0.67^{a,b}	14.37 ± 0.35^{a,b}	4.73 ± 0.05^{a,b}
Vitamins C and E + dichlorvos	326.13 ± 7.44	304.68 ± 7.67	−6.58 ± 0.31^{a,b}	14.33 ± 0.29^{a,b}	4.70 ± 0.06^{a,b}
7th week					
Control	327.30 ± 3.28	363.03 ± 3.91	10.91 ± 0.14	14.62 ± 0.29	4.03 ± 0.04
Vitamins C and E	330.15 ± 1.97	366.70 ± 4.76	11.06 ± 0.80	14.96 ± 0.29	4.08 ± 0.03
Dichlorvos	326.08 ± 6.23	281.98 ± 5.53	−13.44 ± 0.59^{a,b}	17.66 ± 0.57^{a,b}	6.26 ± 0.08^{a,b}
Vitamins C and E + dichlorvos	326.72 ± 6.86	284.15 ± 7.89	−13.04 ± 1.20^{a,b}	17.58 ± 0.41^{a,b}	6.19 ± 0.08^{a,b}

Values are means ± S.D. for six rats in each group. Significance at $P < 0.05$.

[a] Comparison of control and other groups.

[b] Comparison of vitamins C and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups.

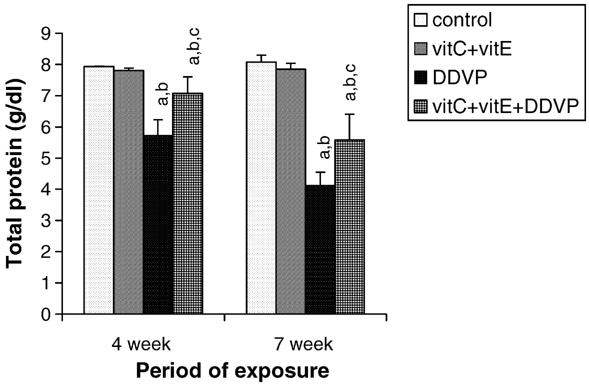

Fig. 1. Serum total protein profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C- and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

Whereas ALP, ALT, AST, GGT, and LDH activities decreased significantly in rats of the vitamins + dichlorvos-treated group compared with the dichlorvos-treated group, total protein and albumin level increased significantly at the end of 4th and 7th week ($P < 0.05$) (Figs. 1–7).

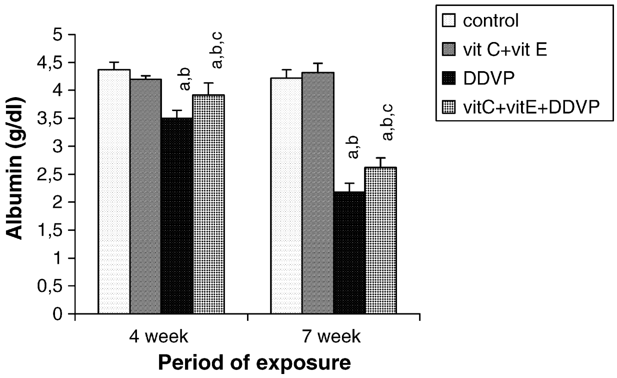

Fig. 2. Serum albumin profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C- and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

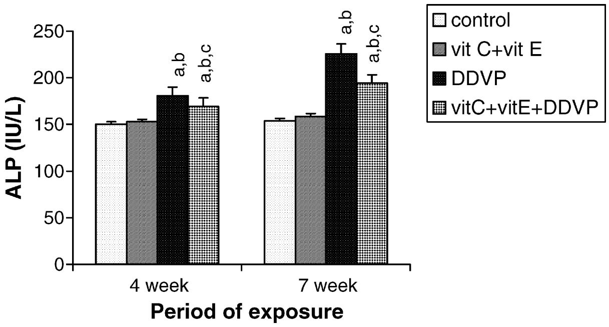

Fig. 3. Serum ALP profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C- and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

3.2.2. *Changes in lipid profile*

At the end of the 4th and 7th week when the dichlorvos- and vitamins + dichlorvos-treated rats were compared with the control group, there was a significant increase in the total cholesterol level and significant decreases in the triglyceride and VLDL-cholesterol levels in both groups of treated rats ($P < 0.05$) (Figs. 8–10).

The total cholesterol level decreased significantly and the triglyceride and VLDL-cholesterol levels increased significantly at the end of the 4th and 7th week in the vitamins + dichlorvos-treated rats compared with the dichlorvos-treated rats ($P < 0.05$) (Figs. 8–10).

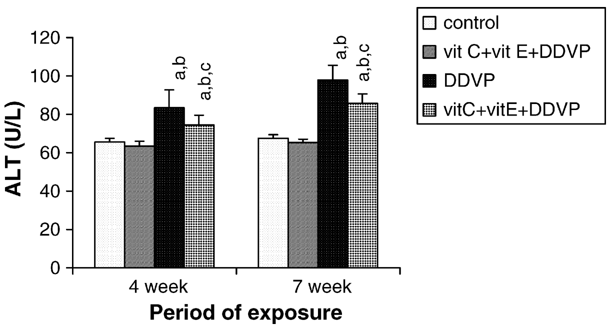

Fig. 4. Serum ALT profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C- and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

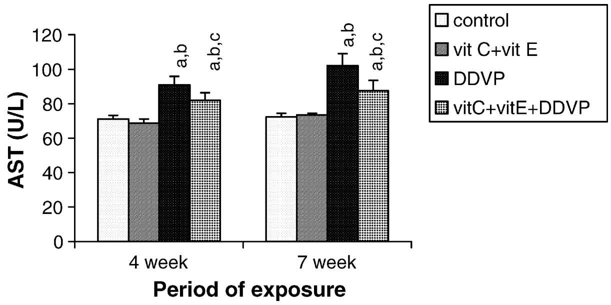

Fig. 5. Serum AST profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C- and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

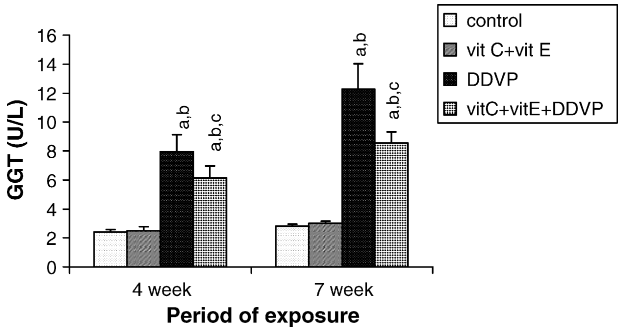

Fig. 6. Serum GGT profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

3.3. *Ultrastructural liver changes*

Hepatocytes of the control rats had a normal structure. Mitochondria and endoplasmic reticulum were abundant in the hepatocytes. The nucleus, which was round and big, was found in the center of the hepatocytes (Fig. 11A).

After 4 weeks of dichlorvos treatment, there was dilatation of the endoplasmic reticulum and the mitochondrial matrix, and cristae were lost (Fig. 11B). After 4 weeks of vitamins + dichlorvos treatment, swelling of the mitochondria and dilatation of the endoplasmic reticulum were observed (Fig. 11C). After 7 weeks of dichlorvos treatment, swelling of the mitochondria, dilatation of the endoplasmic reticulum, loss of cytoplasm, and pyknotic nuclei were observed (Fig. 11D). After 7 weeks of vitamins + dichlorvos treatment, swelling of mitochondria and dilatation of endoplasmic reticulum were observed (Fig. 11E).

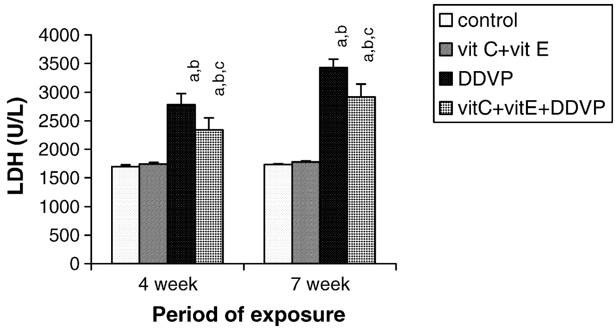

Fig. 7. Serum LDH profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

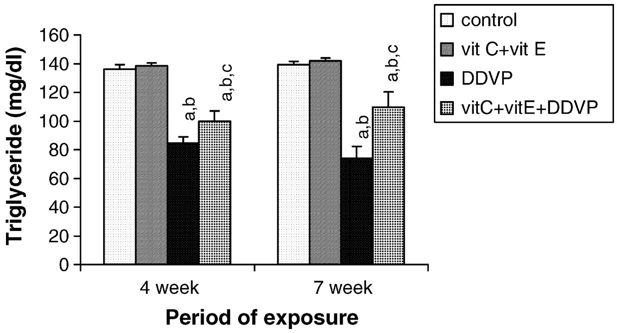

Fig. 8. Serum trigyceride profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

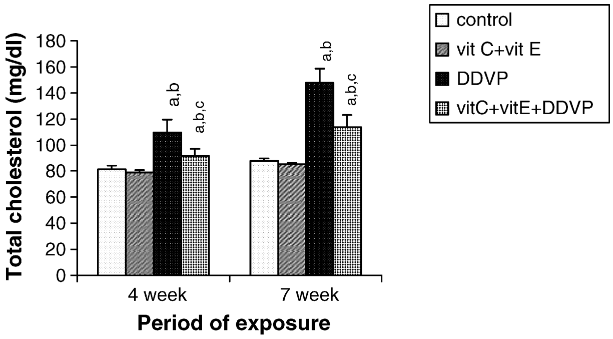

Fig. 9. Serum total cholesterol profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamins C and E + dichlorvos-treated group ($P < 0.05$).

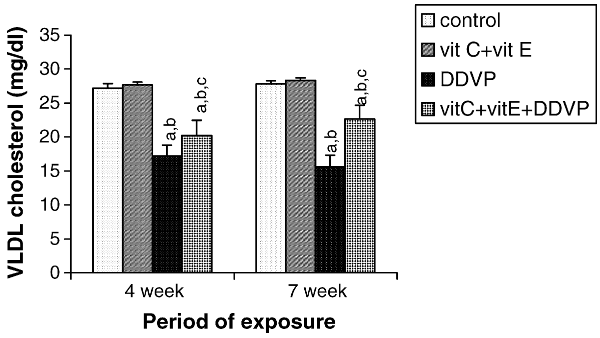

Fig. 10. Serum VLDL-cholesterol profile 4 and 7 weeks after vitamins C and E, dichlorvos and vitamins C and E + dichlorvos treatment to rats. [a]Comparison of control and other groups ($P < 0.05$). [b]Comparison of vitamins C and E-treated group with dichlorvos- and vitamins C and E + dichlorvos-treated groups ($P < 0.05$). [c]Comparison of dichlorvos-treated group with vitamin C and E + dichlorvos-treated group ($P < 0.05$).

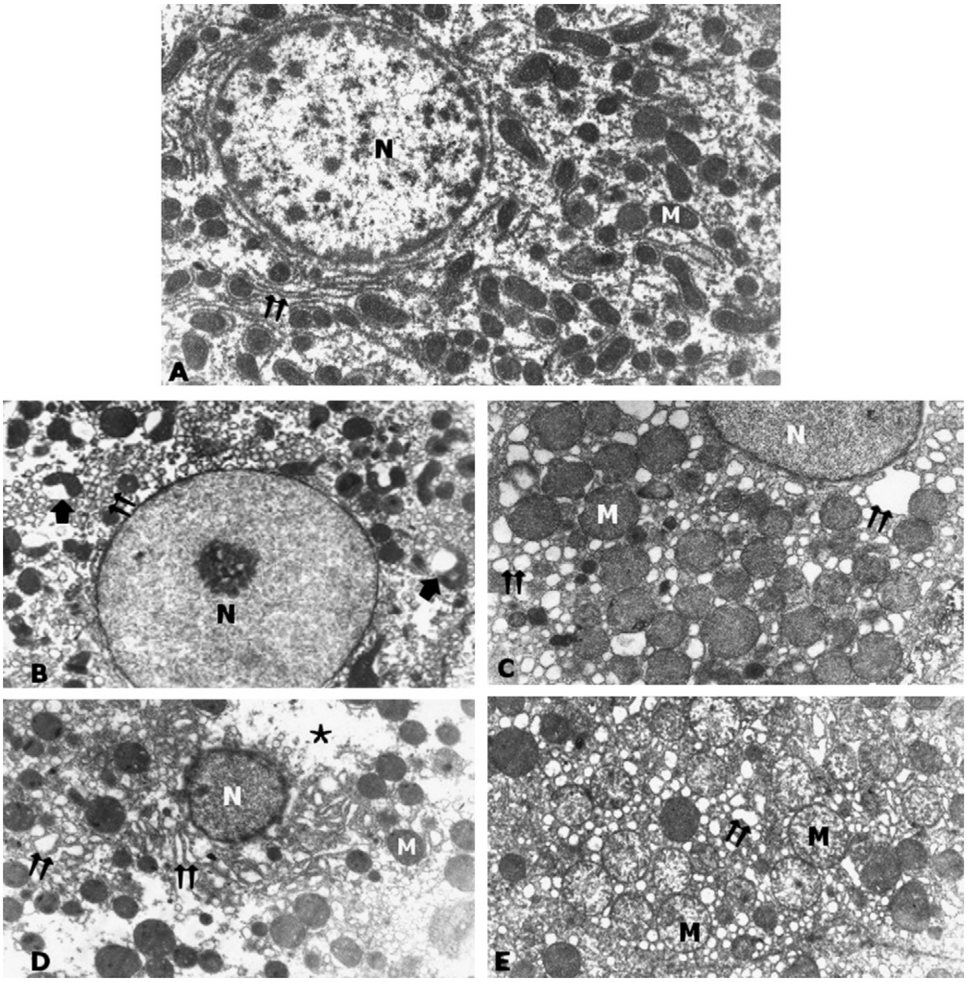

Fig. 11. (A) Electron micrograph of hepatocyte in control rat liver. N: nucleus; M: mitochondria; ⇉: endoplasmic reticulum, 7500×. (B) Lost of mitochondrial matrix and cristae (➡), dilatation of endoplasmic reticulum (⇉) in hepatocyte 4 weeks after dichlorvos treatment to rats, N: nucleus, 7500×. (C) Swelling of mitochondria (M) and dilatation of endoplasmic reticulum (⇉) in hepatocyte 4 weeks after vitamins C and E + dichlorvos treatment to rats, N: nucleus, 10,000×. (D) Swelling of mitochondria (M) and dilatation of endoplasmic reticulum (⇉), lost of cytoplasm (★), picnotic nucleus (N) in hepatocyte 7 weeks after dichlorvos treatment to rats, 10,000×. (E) Swelling of mitochondri (M) and dilatation of endoplasmic reticulum (⇉) in hepatocyte 7 weeks after vitamins C and E + dichlorvos treatment to rats, 10,000×.

4. Discussion

Dichlorvos, an organophosphate, primarily acts by irreversibly inhibiting AChE at cholinergic junctions of the nervous system (Petroianu et al., 2006), which produces hepatotoxicity in rats and induces oxidative stress (Gupta et al., 2005). Dichlorvos is taken into the human body very rapidly by the lungs, stomach, or skin (Güloglu et al., 2004). Dichlorvos not only has toxic effects on mammals but also has toxic effects on fish, birds, honey bees, and non-target invertebrates (Ural and Köprücü, 2006). The oral LD_{50} of dichlorvos is 80 mg/kg for male rats (Okamura et al., 2005).

Okamura et al. (2005) gave 1 mg/kg or 4 mg/kg dichlorvos subcutaneously to rats and observed a decrease in sperm motility. Oral et al. (2006) gave 4 mg/kg dichlorvos orally to rats and observed endometrial damage. In the present study, even though dichlorvos was given at 1/50 LD_{50} oral dose, we observed pathological changes in hepatocytes; however, no rats died during the experimental period.

OP insecticides cause a reduction of body weight in experimental animals (Uzunhisarcikli et al., 2007; Kalender et al., 2007). In the present study, at the end of 4th and 7th week, there was a decrease in the body weight of the dichlorvos- and vitamins + dichlorvos-treated rats compared to the controls. We hypothesize that this decrease occurred as a consequence of reduced food intake.

In addition, at the end of 4th and 7th week, there was an increase in the absolute and relative liver weights of the dichlorvos- and vitamins + dichlorvos-treated rats. OP pesticides cause an increase in the absolute liver weight (Sharma et al., 2005; Jeong et al., 2006) and relative liver weights (Undeger et al., 2000; Johnson et al., 2002; Kang et al., 2004) in experimental animals. Amacher et al. (1998) reported that the increased liver weight was related to enzyme induction of cytochrome-p450. Johnson et al. (2002) stated that the increase in liver weight stemmed from a metabolic reaction induced by the OP. Increases in liver weight might be due to edema in the tissue. Vitamins C and E did not show a protective effect on body weight, absolute liver weight, or relative liver weight.

In this study, at the end of 4th and 7th week, a decrease was observed in the total protein and albumin levels. The results of the present study suggest that exposure to an OP insecticide, such as dichlorvos, may influence total protein and albumin metabolism. Albumin is synthesized by the liver and often transports or binds drugs or chemicals. The albumin level may decrease in individuals that develop liver function disorders after dichlorvos treatment.

OP insecticides may cause increases in the enzymatic activities of ALP, ALT, AST, GGT, and LDH (Morowati, 1997; Srivastava and Raizada, 1999; Banerjee et al., 1999; Gomes et al., 1999; Altuntaş and Delibaş, 2002; Khan et al., 2005; S. Kalender et al., 2005). Changes in the levels of these enzymes may differ depending on the exposure time and dose of dichlorvos. In our study, 4 and 7 weeks after diclorvos administration, ALP, ALT, AST, GGT, and LDH activities increased compared to those of the control group. These changes were magnified over time. ALP, ALT, AST, GGT, and LDH enzymes are primarily used to evaluate hepatic damage. These enzymes are secreted into the blood after hepatocellular injury, resulting in an increase their levels. The electron microscopic findings show that damage occurred to hepatocytes, and the biochemical studies show that the enzyme activities increased.

OP insecticides generally cause an increase in total cholesterol and total lipid levels (Hassan et al., 1988; S. Kalender et al., 2005). Dichlorvos causes an increase in the total cholesterol level of rats (Lucic et al., 2002). In this study, dichlorvos caused an increase in the total cholesterol level. Increased serum cholesterol can be attributed to the effects of the pesticide on the permeability of liver cell membranes (Adham et al., 1997). Also, the increase in the level of serum total cholesterol may be attributed to the blockage of the liver bile ducts, causing a reduction or cessation of cholesterol secretion into the duodenum (Zaahkouk et al., 2000). The present study supports the results of other investigations. An increase in the serum cholesterol level may be a sign of liver damage. Some pesticides cause a decrease in the VLDL-cholesterol and triglyceride levels (Joshi et al., 2003; S. Kalender et al., 2005). Clinically, in parenchymal liver diseases, triglyceride and VLDL-cholesterol levels decrease. In the present study, dichlorvos caused decreases in the triglyceride and VLDL-cholesterol levels. The electron microscopic findings show that damage occurred to the liver cells.

Vitamin E is a potential antioxidant and a lipid-soluble vitamin that is present in biological membranes. Vitamin C could serve to scavenge free radicals within the extracellular space, whereas lipid-soluble vitamin E would effectively scavenge free radicals within cells where reactive metabolites are being produced. In addition, vitamin C may remove free radicals that are bound to vitamin E; thus, vitamin C may serve to regenerate vitamin E (Senthil Kumar et al., 2004). In our study, all of the biochemical parameters assessed after vitamins + dichlorvos treatment were statistically different when compared with those of the control group. All of the biochemical indices were significantly different when the vitamins + dichlorvos-treated group were compared to the dichlorvos-treated group. These results indicate that administration of these vitamins resulted in an improvement in the biochemical indices.

The electron microscopic findings support the biochemical studies. Moussa and Hafez (1995) showed that dimethoate, which is an OP insecticide, inhibited mitochondrial enzyme activity. S. Kalender et al. (2005) reported that an OP insecticide, diazinon, caused swelling of mitochondria in rat hepatocytes. In the present study, dichlorvos caused swelling of mitochondria. Mitochondrial changes in OP-intoxicated animals are indicative of the increased energy requirements necessary for the cells to overcome the toxic effects of the OP compound (S. Kalender et al., 2005; Ogutcu et al., 2006). Also, the same pathological changes were observed in the vitamins + dichlorvos-treated rats.

In present study, we have shown that dichlorvos causes subacute and subchronic hepatotoxicity. Vitamins C and E decreased dichlorvos toxicity, but did not confer complete protection.

Conflict of interest

None.

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